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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,694	08/13/2001	Jan C. Simon	24741-1525	1918

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EXAMINER	
DAVIS, RUTH A	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 05/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,694	SIMON ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-56* is/are pending in the application.

4a) Of the above claim(s) *55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-54 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *55* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment has been received and entered into the case. Claims 20 – 35 have been cancelled, claims 40 – 56 have been added and are pending.

Election/Restrictions

1. Newly submitted claim 55 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The new method of inhibiting keratinocyte cell proliferation is not connected in design, operation, and/or effect. The method is independent since it is not disclosed as capable of use together, has different modes of operation, different functions, and/or different effects than the originally elected method. One would not have to practice the various methods at the same time to practice just one method alone.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 55 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 40 – 45 and 47 – 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 40 – 45 and 47 – 49 are drawn to methods for treating conditions, however are rendered vague and indefinite for reciting "per ml" and "per microliter" because it is unclear to what the volumes refer. For example, in claim 40, the effective amount is 15 micrograms per ml of what?

Claim 49 is rendered vague and indefinite for reciting "in plasma" because it is unclear if the effective amount is based on how much is in the blood after administration or if the amount is 50 micrograms before administration.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claim 46 is rejected under 35 U.S.C. 102(b) as being anticipated by Valavichyus et al. (1986).

Applicant claims a method of treating cancer comprising administering to a subject in need thereof, an effective amount of a composition comprising hyperforin and a pharmaceutically acceptable carrier.

Valavichyus teaches extracts of St. John's Wort, specifically oil extracts, inhibits growth of sarcoma (cancer) cells (abstract). Valavichyus also teaches that administration of the extracts inhibited growth of tumors in animals (or subjects in need thereof). At the time the claimed invention was made, it was known in the art that oil preparations of St. John's Wort are hypericin free and contain high concentrations of hyperforin (See Chavez, p.1622). It was also known in the art that plant oils were used as pharmaceutical carriers.

Applicant argues that Valavichyus uses a combination of St. John's and chamomile making it unclear which agent is the effective agent and that the effective volumes and concentrations of hyperforin are not disclosed.

However, these arguments fail to persuade because the claimed method comprises administering a composition comprising hyperforin, which includes other ingredients in addition to the hyperforin. The reference specifically teaches administering a composition comprising an oil extract of St. John's Wort (containing hyperforin) for treating cancer, as instantly claimed. In addition, the claim does not recite effective volumes or concentrations. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. Thus, the argument is not commensurate with the scope of the claim. Therefore, the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 36 and 39 – 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over The Hypericum Home Page (1996).

Applicant claims a method for treating a condition selected from cancer, inflammatory skin diseases, precancerous conditions, geriatric skin or microbial skin infections comprising topical administration of an effective amount of a composition consisting of (a) pharmaceutically acceptable carrier and (b) an active agent consisting of (i) hyperforin or (ii) hyperforin and hypericin, to a subject in need thereof. Specifically, the subject is a mammal and the composition is a topical ointment with an effective amount of at least 15 micrograms hyperforin per ml, 0.02 – 20 mg/ml, 1 – 20 mg/ml, 10 mg/ml, 15 micrograms/ml, or 20 – 150 micrograms/ml.

The Hypericum Home Page (HHP) teaches extracts of Hypericum perforatum (St. John's Wort) include hypericin and hyperforin wherein the extracts exhibit anti-inflammatory and

antibacterial effects when externally, or topically, applied (p.3). HHP specifically teaches that hyperforin is attributed with anti-inflammatory and antibacterial effects (p.3).

HHP does not teach a method for treating an anti-inflammatory condition with the claimed effective amounts. However at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to use hyperforin in a method for treating anti-inflammatory conditions because of the disclosed anti-inflammatory effect. In addition, it would have been obvious to one of ordinary skill in the art to optimize effective volumes and concentrations as it was routinely practiced in the art at the time the claimed invention was made. It would have been further obvious to one of ordinary skill in the art to include a pharmaceutical carrier because it was routine practice in the art at the time the claimed invention was made. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated to use hyperforin in a method for treating anti-inflammatory conditions with a reasonable expectation of success because of its known benefit as disclosed by HHP.

Applicant argues that HHP teaches in vitro activity and does not mention hyperforin. However, this argument fails to persuade because as stated above, HHP specifically attributes hyperforin with the anti-inflammatory action when topically applied to patients (p.3).

9. Claims 36 – 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over The Hypericum Home Page (1996) in view of The Merck Manual.

Applicant claims a method for treating a condition selected from cancer, inflammatory skin diseases, precancerous conditions, geriatric skin or microbial skin infections comprising topical administration of an effective amount of a composition consisting of (a) pharmaceutically

acceptable carrier and (b) an active agent consisting of (i) hyperforin or (ii) hyperforin and hypericin, to a subject in need thereof. Specifically, the subject is a mammal and the condition is eczema, or alternatively, the condition is selected from exsiccation eczema, hyperkeratotic hand and foot eczema, contact eczema, atopic dermatitis, neurodermatitis, lichen simplex, prurigo simplex, lymphoma, leukemia, melanoma, epithelial precancerous conditions, tumor metastases or epithelial tumor.

The Hypericum Home Page (HHP) teaches extracts of Hypericum perforatum (St. John's Wort) include hypericin and hyperforin wherein the extracts exhibit anti-inflammatory and antibacterial effects when externally, or topically, applied (p.3). HHP specifically teaches that hyperforin is attributed with anti-inflammatory and antibacterial effects (p.3).

HHP does not teach a method for treating an anti-inflammatory condition with the claimed effective amounts. However at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to use hyperforin in a method for treating anti-inflammatory conditions because of the disclosed anti-inflammatory effect. In addition, it would have been obvious to one of ordinary skill in the art to optimize effective volumes and concentrations as it was routinely practiced in the art at the time the claimed invention was made. It would have been further obvious to one of ordinary skill in the art to include a pharmaceutical carrier because it was routine practice in the art at the time the claimed invention was made. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated to use hyperforin in a method for treating anti-inflammatory conditions with a reasonable expectation of success because of its known benefit as disclosed by HHP.

HHP does not teach the extracts are effective against eczema, or other conditions as claimed. However, at the time of the claimed invention, it was well known in the art that eczemas are characterized by inflammation (See "The Merck Manual", cited on PTO-892). Specifically, eczema, contact eczema, atopic eczema, hand and foot eczemas, and lichen simplex are each characterized as superficial inflammations of the skin of varying degrees. At the time of the invention, it would have been obvious to one of ordinary skill in the art to treat any of the aforementioned eczemas with hyperforin because of the disclosed anti-inflammatory effect as disclosed by HHP. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by HHP and Merck to utilize hyperforin in a method for treating inflammation and eczemas with a reasonable expectation for success.

Applicant argues that HHP teaches in vitro activity and does not mention hyperforin. However, this argument fails to persuade because as stated above, HHP specifically attributes hyperforin with the anti-inflammatory action when topically applied to patients (or mammals) (p.3).

10. Claims 46 – 49 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valavichyus (1986).

Applicant claims a method of treating cancer comprising administering to a subject in need thereof an effective amount of a composition comprising hyperforin and a pharmaceutically acceptable carrier. Specifically, the effective amount comprises at least 50 micrograms hyperforin/ml in an injectable form, 100 micrograms/microliter suitable for epicutaneous

application, 50 micrograms/ml for systemic administration and the hyperforin is at least 90% pure.

Valavichyus teaches extracts of St. John's Wort, specifically oil extracts, inhibits growth of sarcoma (cancer) cells (abstract). Valavichyus also teaches that administration of the extracts inhibited growth of tumors in animals (or subjects in need thereof). At the time the claimed invention was made, it was known in the art that oil preparations of St. John's Wort are hypericin free and contain high concentrations of hyperforin (See Chavez, p.1622). It was also known in the art that plant oils were used as pharmaceutical carriers.

Valavichyus does not teach the method wherein the claimed volumes and concentrations were used, or wherein the hyperforin is at least 90% pure. However, it would have been obvious to one of ordinary skill in the art to optimize effective volumes and purity of effective agents because it was routinely practiced in the art at the time the claimed invention was made. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the effective amounts of Valavichyus with a reasonable expectation for successfully treating cancer.

Applicant argues that Valavichyus uses a combination of St. John's and chamomile making it unclear which agent is the effective agent and that the effective volumes and concentrations of hyperforin are not disclosed.

However, these arguments fail to persuade because the claimed method comprises administering a composition comprising hyperforin, which includes other ingredients in addition to the hyperforin. The reference specifically teaches administering a composition comprising an oil extract of St. John's Wort (containing hyperforin) for treating cancer, as instantly claimed.

Furthermore, although the reference does not teach the claimed effective concentrations, it would have been obvious to one of ordinary skill in the art to optimize such effective amounts as it was routinely practice in the art at the time claimed invention was made.

11. Claims 46 – 54 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valavichyus in view of The Hypericum Homepage (1996) and DeCosterd et al. (Helv Chim Acta, 1989).

Applicant claims a method of treating cancer comprising administering to a subject in need thereof an effective amount of a composition comprising hyperforin and a pharmaceutically acceptable carrier. Specifically, the effective amount comprises at least 50 micrograms hyperforin/ml in an injectable form, 100 micrograms/microliter suitable for epicutaneous application, 50 micrograms/ml for systemic administration and the hyperforin is at least 90% pure. The cancer is melanoma, lymphoma, skin cancer, mammary carcinoma and leukemia carcinoma.

Valavichyus teaches extracts of St. John's Wort, specifically oil extracts, inhibits growth of sarcoma (cancer) cells (abstract). Valavichyus also teaches that administration of the extracts inhibited growth of tumors in animals (or subjects in need thereof). At the time the claimed invention was made, it was known in the art that oil preparations of St. John's Wort are hypericin free and contain high concentrations of hyperforin (See Chavez, p.1622). It was also known in the art that plant oils were used as pharmaceutical carriers.

Valavichyus does not teach the method wherein the claimed volumes and concentrations were used, or wherein the hyperforin is at least 90% pure. However, it would have been obvious

to one of ordinary skill in the art to optimize effective volumes and purity of effective agents because it was routinely practiced in the art at the time the claimed invention was made. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the effective amounts of Valavichyus with a reasonable expectation for successfully treating cancer.

Valavichyus does not teach the method wherein the cancer is melanoma, lymphoma, skin cancer, mammary carcinoma and leukemia carcinoma. However, HHP teaches extracts of Hypericum perforatum (St. John's Wort) include hypericin and hyperforin wherein the extracts demonstrate anticancer properties and have been proven to inhibit tumor cells of the brain, lung and skin (p.4). In addition, DeCosterd teaches extracts of Hypericum inhibit growth of colon carcinomas (abstract). Specifically, DeCosterd teaches derivatives of hyperforin exhibit the growth-inhibiting activity (abstract). As evidenced by the cited references, at the time of the invention, hyperforin, derivatives thereof and extracts of Hypericum were well known as effective agents against cancers of various kinds. Although each of the references do not specifically teach the agents in methods for treating a subject in need thereof, they do suggest that such activity would be expected. Therefore, one of ordinary skill in the art would have been motivated to use the extracts in treating cancers (i.e. lymphoma, mammary and leukemia carcinomas) because of the demonstrated effectiveness in a variety of cancers as disclosed by the references above. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by HHP and/or DeCosterd to use compositions comprising hyperforin or hyperforin and hypericin in the methods for treating various cancers with a reasonable expectation of success.

Applicant argues that Valavichyus uses a combination of St. John's and chamomile making it unclear which agent is the effective agent and that the effective volumes and concentrations of hyperforin are not disclosed.

However, these arguments fail to persuade because the claimed method comprises administering a composition comprising hyperforin, which includes other ingredients in addition to the hyperforin. The reference specifically teaches administering a composition comprising an oil extract of St. John's Wort (containing hyperforin) for treating cancer, as instantly claimed. Furthermore, although the reference does not teach the claimed effective concentrations, it would have been obvious to one of ordinary skill in the art to optimize such effective amounts, as it was routinely practice in the art at the time claimed invention was made.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
April 29, 2002

LEONARD LANKFORD, JR
PRIMARY EXAMINER